ERYTHROCYTOSIS IN ARTIFICIALLY-INOCULATED MALARIA

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In eleven cases of general paralysis inoculated subcutaneously with benign tertian malarial blood, Pijper and Russell (1925) found that an erythrocytosis occurred before the anaemia developed. In the graph showing the mean of the daily observations on these cases, the increase of the red cells occurs before the onset of the fever and is to the extent of about 750,000 cells per c.mm. In the charts of two cases, however, the erythrocytosis is shown to persist until the eleventh and twelfth days of the fever. The greatest increase recorded by these observers was 2,000,000 cells per c.mm.

On the other hand, R. M. Gordon (1925) found no increase of the red cells in three general paralytics inoculated with benign tertian malaria by means of anopheline mosquitos. Ben-Harel (1923) found in a series of 23 blood inoculations of *Proteosoma praecox*, in canaries, that the red cells diminished in numbers before the parasites were found in the blood stream.

The observations described in this paper were made upon cases of general paralysis inoculated with benign tertian malaria at Claybury Mental Hospital. Case No. 1 was inoculated by means of anopheline mosquitos by Lieut.-Col. S. P. James. The other cases were inoculated with defibrinated malarial blood by means of the method described by one of us elsewhere (1925). Cases Nos. 1 and 2 were females, 62 and 42 years of age ; cases Nos. 3 and 4 were males, 40 and 50 years of age.

The red cell estimations were made with the Thoma-Zeiss counting apparatus and the haemoglobin estimations by means of Oliver's haemoglobinometer. The blood was collected between 9.30 a.m. and 10 a.m. every day from cases Nos. 1 and 2, and at 5.30 p.m. from

cases Nos. 3 and 4. Three red cell counts were performed in cases Nos. 3 and 4, the averages being taken as the correct readings. In cases Nos. 1 and 2 the red cell count was invariably repeated several times if there was much variation from the previous day's count. The average was taken of the two counts which approached each other most nearly. These methods of counting the red cells were used on account of the great error there is in the usual red cell count, Gordon (1925) placing it at 500,000 cells per c.mm. The temperature of each patient was recorded every four hours unless it was above normal; it was then recorded each hour until normal was regained. No drugs, other than those mentioned on the charts, were given.

Red Cells. The results obtained from the red cell counts are shown on the charts. All four cases show very clearly an erythrocytosis preceding the anaemia. The relation of this increase of the red cells to the onset of the fever was very variable. In case No. 1 it occurred before and during the onset, in case No. 2 it coincided with the onset, in case No. 3 the greatest increase occurred after the fifth rise of temperature and in case No. 4 after the eighth. As the count was not commenced until six days after the onset of the fever in this case, it is possible that there had been an erythrocytosis previous to the one recorded.

This erythrocytosis is in agreement with the findings of Pijper and Russell, but not with those of R. M. Gordon or Ben-Harel. As neither of the two latter workers record observations made every day, it is possible that an erythrocytosis occurred between the observations. Cases Nos. 1 and 2 of the present series show that the erythrocytosis may persist for only a few days. Gordon does, however, describe one case on whom red cell counts were performed every day, but the estimations were not commenced until the ninth day of infection. There were then 6,000,000 red cells per c.mm. As this is a comparatively high figure for an untreated general paralytic in England, perhaps the count represents an erythrocytosis. In case No. 1 of the present series, 6,000,000 red cells per c.mm. were found on the tenth day of infection.

The duration of the anaemia is of interest. In cases Nos. 1 and 3 it persisted for at least 11 and 13 days after the commencement of the quinine. In case No. 4 it persisted for at least six days after the course of quinine had been started, becoming more

profound although no further febrile paroxysms had occurred. This case corresponds with one described by Gordon. In this patient, a female aged 13 years, the red cells continued to fall although the parasites had disappeared from the peripheral blood. In case No. 4 of the present series the same condition occurred. The lowest red cell count found in the present series was 1,300,000 cells per c.mm.

Recovery from the anaemia took place in a comparatively short time. In cases Nos. 1, 2 and 3, the red cells reached 5,000,000 per c.mm. in about three weeks. During this period the cells increased by 1,700,000 per c.mm. in case No. 1, by 2,600,000 per c.mm. in case No. 3, and by 3,300,000 per c.mm. in case No. 2. In these cases the degree of the anaemia did not influence the time required for normal to be regained. James (1920) gives a chart, after Ziemann, showing regeneration of the red cells after naturally-acquired malaria. In this case the normal was regained 16 days after the anaemia. Case No. 4 shows a more rapid recovery, 5,000,000 red cells per c.mm. being reached in about a week after the anaemia. In cases Nos. 1 and 2, both of whom received neo-kharsivan in addition to quinine, the regeneration of the red cells was no more rapid than in case No. 3, and less rapid than in case No. 4. Neither of the two latter cases were given this preparation. As neosalvarsan has a definite parasiticidal action on *Plasmodium vivax*, both in the naturally-acquired infection (D'Esterre, 1920; Nieuwenhuyse, 1921; Johnson, Gilchrist and Hay-Michel, 1921) and in the artificially-inoculated form (Pijper and Russell, 1924), it might be expected that the parasites would be destroyed more rapidly in cases Nos. 1 and 2, than in cases Nos. 3 and 4 and, consequently, the red cells would be regenerated more rapidly. This did not occur.

In cases Nos. 3 and 4, red cell counts were continued after the normal had been regained. In each case an erythrocytosis was found. The highest count obtained in case No. 3 was 5,920,000 cells per c.mm., and in case No. 4, 6,280,000 per c.mm. This post-anaemia increase of red cells has been observed, according to Ben-Harel, in the naturally-acquired infection, and this worker noted it in canaries who had suffered from infection with *Proteosoma praecox*. In two of the birds the erythrocytosis persisted for a little over six

months. Of the two cases under review, No. 3 showed a count of 4,990,000 cells per c.mm., with a haemoglobin percentage of 65 on July 10th, nearly six months after the last rigor, while No. 4 gave a count of 5,870,000 cells per c.mm. and haemoglobin at 90 per cent. on July 22nd, exactly six months after the last rigor. Although the highest point reached in these two cases was not permanent, in neither case was the count lower than it had been before the malarial anaemia. In case No. 4 it was about one million higher.

Haemoglobin and Colour-Index. In cases Nos. 3 and 4 estimations were made of the haemoglobin. The results, with the colour-indices, are shown on the charts. The haemoglobin does not vary to the same extent as do the red cells and the colour-index remains low. The colour-index in case No. 4 is of the secondary anaemia type throughout. This corresponds with the two cases reported by Gordon. This agreement is not seen in case No. 3, for the index exceeds unity on two occasions in this patient. In both cases it falls very low at certain periods.

Number of Parasites. In cases Nos. 1 and 2 the relative number of parasites was found by counting the total number of asexual forms in 100 fields of the microscope, using 1/12th in. oil-immersion objective and thin blood-films. Although the actual number of asexual parasites was very different in the two cases, both patients show that there is a tendency for the temperature to vary with the number of parasites in each patient. The temperatures of the two cases were recorded every hour when above normal, at other periods every four hours. In the cases investigated by Pijper and Russell the temperatures were recorded every four hours throughout. In their cases there is no clear relationship between the number of parasites and the degree of fever.

Previous Malaria. Three of Pijper and Russell's nine cases were known to have had previous attacks of malaria, whilst the remainder had a doubtful history with regard to this point. Of the present series, cases Nos. 1 and 2 are known not to have suffered from the infection previously. It is clear, therefore, that the increase of the red cells preceding the anaemia does not necessarily bear any relation to previous malaria, for the increase was found both in patients who had suffered from previous malaria and in those who had not.

Sex. As the increase of the red cells preceding the anaemia was found in both female (Nos. 1 and 2) and male (Nos. 3 and 4) cases, the erythrocytosis is not dependent upon the sex of the patient.

Mode of Inoculation. Case No. 1 was inoculated by means of anopheline mosquitos, the remaining patients by means of subcutaneous injection of malarial blood. Pijper and Russell's cases were inoculated by the latter method. The pre-anaemia erythrocytosis was found in all the cases. The increase of the red cells is not dependent upon the method of inoculation, therefore, so far as these two methods are concerned.

SUMMARY

(1) In four cases of general paralysis inoculated with benign tertian malaria an erythrocytosis was found to precede the anaemia. The erythrocytosis occurred whether the inoculation was performed by means of mosquitos or by subcutaneous injection of malarial blood. It was independent of the sex of the patient and of a history of previous malaria. The succeeding anaemia occurred, or persisted for several days after the cessation of the fever. Regeneration of the red cells was complete within three weeks, although the degree of anaemia was very different in the four cases. An erythrocytosis was found to follow the anaemia.

(2) The haemoglobin was found, in two cases, to vary with the red cells, but regeneration was less rapid. The colour-index was, as a rule, of the secondary anaemia type. At certain periods it became as low as ·5.

(3) In two cases the number of parasites was found to vary approximately with the degree of fever, although the number of parasites was very different in the two cases.

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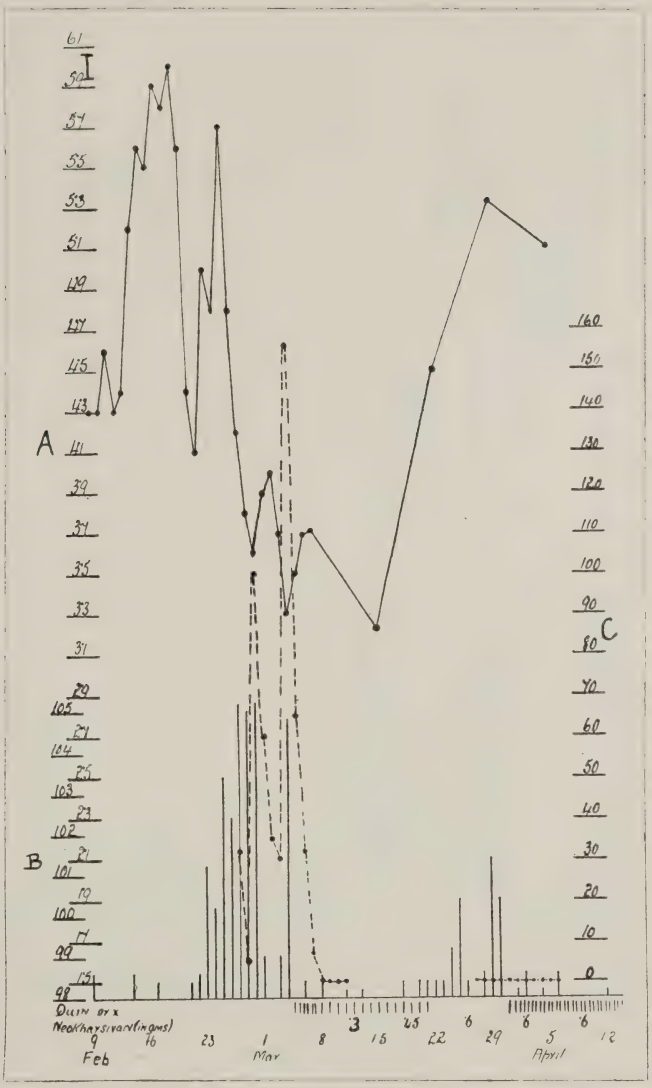
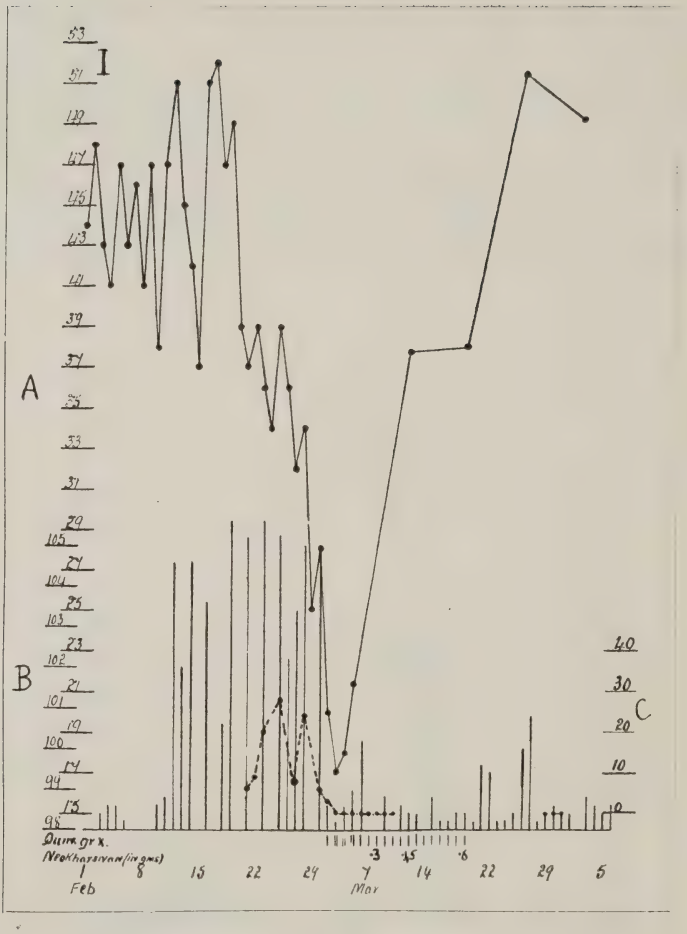
EXPLANATION OF CHARTS

A. Number of red cells in millions per c.mm.
B. Temperature in degrees, Fahrenheit.
C. Number of parasites in 100 fields.
D. Haemoglobin percentage.
E. Colour-Index.
I. Day of Inoculation.

Red cells ———
Parasites – – – – – – and ▬▬▬
Haemoglobin – – – – – – –
Colour-index .....
Temperature |



Case No. 1



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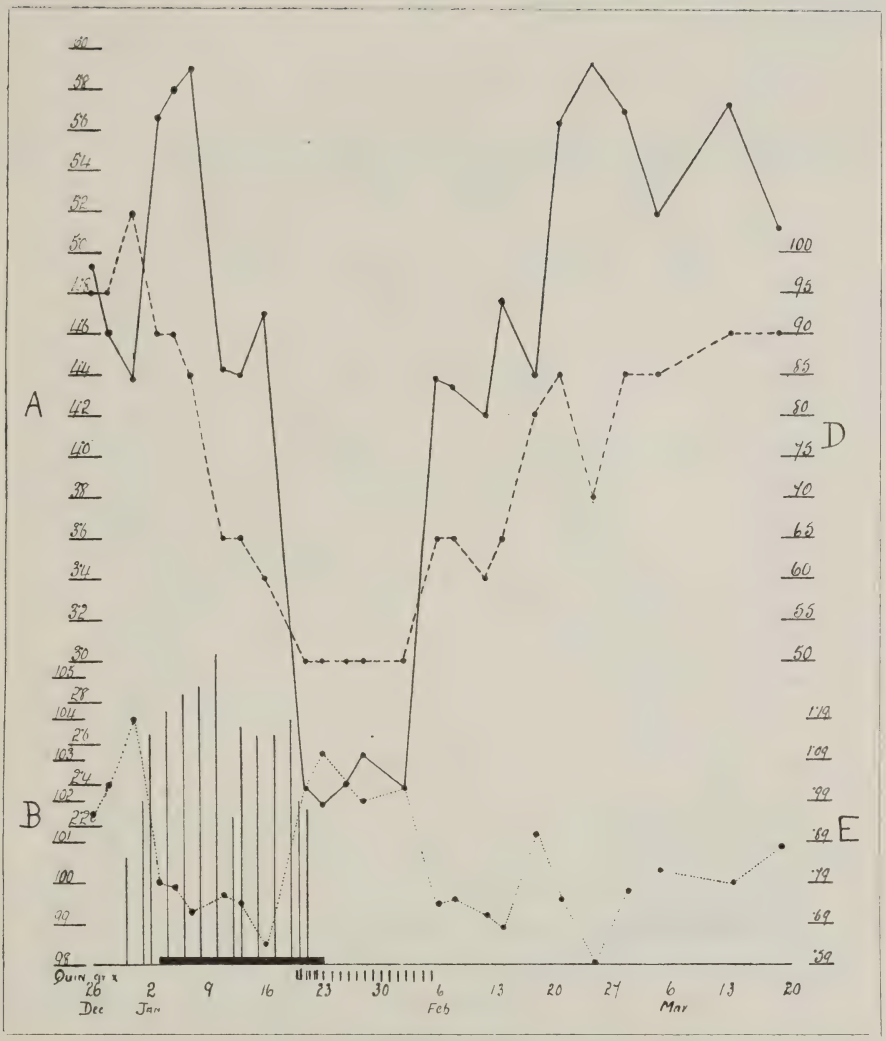
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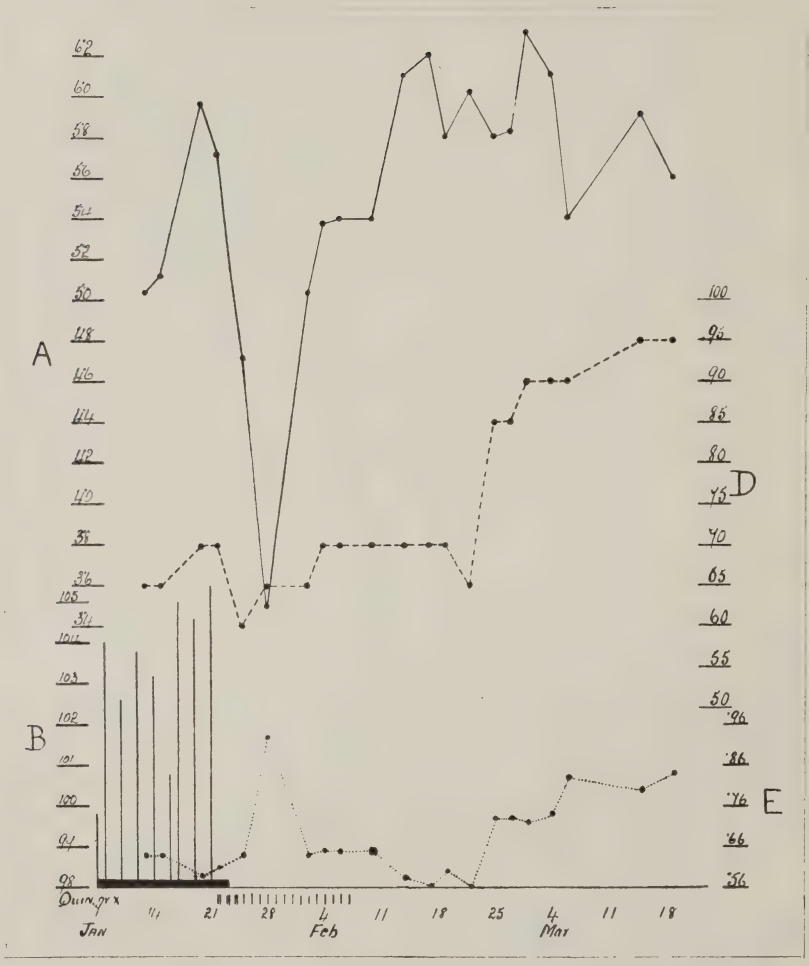
Case No. 3



Case No. 4